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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,146	05/26/2006	Alexander A. Khromykh	45930.5.1	9049

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EXAMINER	
BOESEN, AGNIESZKA	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/559,146	KHROMYKH, ALEXANDER A.	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16-25 and 27-39* is/are pending in the application.

4a) Of the above claim(s) *29-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,16-25,27,28 and 35-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/23/2009 and 2/20/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed 9/23/2008 and 1/29/2009 in response to the Office Action of 6/23/2008 is acknowledged and has been entered. Claims 14 and 25 have been amended. Claims 15 and 26 have been canceled. Rejections of canceled claims are moot. New claims 38 and 39 have been added. Claims 29-34 are withdrawn. Claims 1-14, 16-25, 27, 28, and 35-39 are under Examination in this Office action.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 9/23/2008 and 2/20/2009 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the Examiner.

Claim Rejections - 35 USC § 112

Rejection of claims 1-5, 7-10, 12-25, 27, 28, and 35-37 under 35 U.S.C. 112, first paragraph, **is withdrawn** in view of Applicant's arguments and amendments to the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of claims 2, 3, 8, 16, 17 and 36 under 35 U.S.C. 102(b) as being anticipated by Khromykh (WO/03/046189A1 in IDS of 12/05/2005) **is withdrawn** in view of Applicant's arguments.

Rejection of claims 1, 4-7, 9-14, 18-25, 27, 28, 35 and 3 under 35 U.S.C. 102(b) as being anticipated by Khromykh (WO/03/046189A1 in IDS of 12/05/2005) **is maintained**. **New claims 38 and 39 are rejected as being anticipated by Khromykh (WO/03/046189A1 in IDS of 12/05/2005).**

Regarding claims 38 and 39: Khromykh discloses Kunjin virus VLPs encoding and expressing a protein translation product comprising C protein, prM protein and E protein (see claims 1-5, 10-16, 24, and 25, Figures 10 and 11, Table 5, page 12, lines 24-29, page 14, lines 19-23, page 34, lines 19-25). The Kunjin virus VLP disclosed by Khromykh is in RNA form and encodes a heterologous nucleic acid encoding murine epitopes (see page 5, lines 25-30, page 10, lines 10-20, Figures 2, 3 and 11).

The flaviviral packaging system disclosed by Khromykh comprises mutations in nonstructural proteins: Leucine residue 250 substituted by Proline in the NS 1 nonstructural protein, (ii) Alanine 30 substituted by Proline in the nonstructural protein NS2A; (iii) Asparagine 101 substituted by Aspartate in the nonstructural protein NS2A; and (iv) Proline 270 substituted by Serine in the nonstructural protein NS5 (see claim 4, page 5, lines 1-15 and page 16, lines 1-10).

Khromykh teaches CMV promoter and the IRESNeo selection marker (see page 9, lines 1-25, page 18, lines 10-15 and page 32, lines 30-31 and Figure 11). Khromykh teaches the BHK21 host cell (see page 18, lines 23-29, and Examples 1 and 4).

Khromykh teaches an immunogenic composition comprising flavivirus VLP encoding C protein, prM protein and E protein and a heterologous protein (see claims 36-50). It is noted that the claims are rejected for the enabled embodiment of the immunogenic composition.

Khromykh teaches methods of producing flavivirus VLPs and methods of producing a recombinant protein by infecting a mammalian host cell with the flaviviral replicon, producing VLPs and infecting a second host cell (see Example 1 and Results on pages 29-32).

Response to Applicant's arguments

Applicant's arguments have been fully considered but fail to persuade. Applicant acknowledges that Figure 11 of Khromykh discloses a single protein translation product encoding C, prM and E proteins under 26S promoter. Applicant argues that because the construct in Figure 11 was in RNA form, this construct did not and could not comprise CMV promoter. Applicant argues that Figure 10 of Khromykh discloses proteins translation products encoding C, prM and E proteins transcribed under separate promoters.

In response to Applicant's arguments the Examiner notes that the present claims are not limited to the CMV promoter but broadly recite any promoter. Additionally, while some rejected claims recite that the construct is in RNA form other claims broadly recite a construct comprising and encoding the C, prM and E proteins under a promoter. It is noted that claims limited to the tetracycline repressible CMV promoter are presently rejected under 35 USC 103(a)

below. Thus because Khromykh discloses a flavivirus construct comprising the C, prM and E proteins and a operably linked promoter (see Figure 11, page 34 lines 11-25 and Table 5) as required by the present claims Khromykh anticipates the present claims.

New Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 3, 8, 16, 17 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Khromykh (WO/03/046189A1 in IDS of 12/05/2005) as applied to claims 1, 10, and 35 and further in view of Apt et al. (US Patent 7,476,390 B2).

Khromykh teaches Kunjin virus VLPs encoding and expressing a protein translation product comprising C protein, prM protein and E protein (see claims 1-5, 10-16, 24, and 25, Figures 10 and 11, Table 5, page 12, lines 24-29, page 14, lines 19-23, page 34, lines 19-25). The Kunjin virus VLP disclosed by Khromykh is in RNA form and encodes a heterologous nucleic acid encoding murine epitopes (see page 5, lines 25-30, page 10, lines 10-20, Figures 2 and 3).

The flaviviral packaging system disclosed by Khromykh comprises mutations in nonstructural proteins: Leucine residue 250 substituted by Proline in the NS 1 nonstructural protein, (ii) Alanine 30 substituted by Proline in the nonstructural protein NS2A; (iii) Asparagine 101 substituted by Aspartate in the nonstructural protein NS2A; and (iv) Proline 270 substituted

by Serine in the nonstructural protein NS5 (see claim 4, page 5, lines 1-15 and page 16, lines 1-10).

Khromykh teaches CMV promoter and the IRESNeo selection marker (see page 9, lines 1-25, page 18, lines 10-15 and page 32, lines 30-31 and Figure 11). Khromykh teaches the BHK21 host cell (see page 18, lines 23-29, and Examples 1 and 4).

Khromykh teaches an immunogenic composition comprising flavivirus VLP encoding C protein, prM protein and E protein and a heterologous protein (see claims 36-50). It is noted that the claims are rejected for the enabled embodiment of the immunogenic composition.

Khromykh teaches methods of producing flavivirus VLPs and methods of producing a recombinant protein by infecting a host cell with the flaviviral replicon, producing VLPs and infecting a second host cell (see Example 1 and Results on pages 29-32).

While Khromykh teaches a construct comprising C protein, prM protein and E protein and the use of the CMV promoter in other of his constructs, Khromykh does not expressly teach the tetracycline repressible CMV promoter.

Apt teaches expression constructs comprising multiple flavivirus antigens expressed under one CMV promoter (see Figures 1 and 2 and Figure description in columns 17 and 18). Apt teaches that his expression vectors comprise tetracycline as a selectable marker (see column 95, lines 35-41).

It would have been *prima facie* obvious to use Apt's tetracycline repressible CMV promoter in the construct of provide Khromykh because Apt teaches that tetracycline is used as a selectable marker and allows selection for specific genes in the host cells.

The present claims would have been obvious because combining prior art elements, the expression construct taught by Khromykh and Apt's tetracycline repressible CMV promoter would have yielded predictable results to one of ordinary skill in the art at the time of the invention (i.e using the tetracycline repressible CMV promoter the skilled artisan would have been able to select for genes expressed in the construct). See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Rejection of claims 1-26 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No 6,893,866 B1 **is withdrawn** in view of Applicant's arguments.

Rejection of claims 1-14 and 16-25 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 66-79 of copending Application No. 11/098,283 **is maintained.**

Rejection of claims 1-14 and 16-25 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 5, 7-10, 12-32, of copending Application No. 11/816,350 **is maintained.**

Applicant requests that the rejections are maintained in order to be considered at a later date.

New Rejections

Claims 1-14, 16-25, 27, 28, and 35-39 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 10, 36, 41-50, and 68-75 of copending Application No. 10/496,421. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the present and the copending Application are drawn to a flavivirus gene expression construct expressing Kunjin virus structural proteins comprising Proline 250 to Leucine substitution mutation in nonstructural protein NS1.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-14, 16-25, 27, 28, and 35-39 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-37 of U.S. Patent No 6,893,866 B1 in view of Apt (US Patent 7,476,390 B2). Although the conflicting claims are

not identical, they are not patentably distinct from each other because both the present claims and claim 1 of the U.S. Patent No 6,893,866 B1 are drawn to an expression vector incapable of producing infectious virus comprising a nucleotide sequence encoding a flavivirus replicon derived from the Kunjin virus, the expression vector comprising the insertion site for heterologous nucleic acid, the expression vector comprising a heterologous nucleic acid, and further comprising a second expression construct that facilitates packaging of the expression construct into flavivirus like particles (VLPs).

US Patent does not expressly disclose the flavivirus construct, wherein the multiple proteins are expressed and translated as a single translation product.

Apt teaches expression constructs comprising multiple flavivirus antigens expressed under one CMV promoter (see Figures 1 and 2 and Figure description in columns 17 and 18).

It would have been *prima facie* obvious to provide Apt's construct expressing all components of the construct of US Patent 6,893,866 B1 under one promoter because expressing a number of proteins under one and the same promoter has been successfully done in the art (as evidenced by Apt).

Applicant argues unexpected results; however Applicant fails to provide the support for the argued unexpected result in the specification. Absent any evidence to the contrary, better expression of proteins under one promoter versus under multiple promoters would have been obvious and expected.

Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AGNIESZKA BOESEN whose telephone number is (571)272-8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/

Examiner, Art Unit 1648